

the submissions that failed to demonstrate efficacy (52%). Characteristics associated with a PFR were being a biologic product, having an appropriate comparator, showing sufficient clinical evidence and being priced at a similar/lower price than the comparator. **CONCLUSIONS:** The presence of patient input was not associated with a PFR. The lack of significant association could be attributed to external factors that are not captured in CADTH's summary reports and the limited sample size of data available. It remains unclear how patient input is integrated into the decision making process.

## HEALTH CARE USE & POLICY STUDIES – Disease Management

### PHP6

#### STUDY OF THE SANITARY GEOGRAPHY OF COLOMBIA: A BIG DATA APPROACH

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**OBJECTIVES:** This study aims to propose a new geographic administrative organization of Colombian municipalities for health care management purposes. Rather than responding to arbitrary political boundaries, this division should answer to health needs and capacities, in order to facilitate the development of targeted policies to reach universal coverage and improve access to health services. **METHODS:** To achieve this, a big database was created: it contains information about different health-affecting topics: economic development, socio-cultural background, public and transportation services, environmental conditions and health indicators, supply and demand. These topics were measured with over 70 variables. After that, using a principal-component analysis, one or two indicators were created per topic. These indicators were used to build clusters that latter allowed the development of sanitary regions. Afterwards, another study was made in which people were tracked from their residence to the places where they received health services. Then, the country was divided into regions reflecting those migration flows. Finally, the study mingles both information -the clusters and migration networks- to determine a sanitary geography of Colombia. **RESULTS:** Using the methodology, this study proposes six clustering methodologies that are statistically significant and consistent with the reality of Colombia. Also, many networks were proposed, but 5 of them represented the national situation closely. Combining these alternatives, the study achieves its goal and creates a satisfactory segmentation of the country that is valuable for public policy. **CONCLUSIONS:** The proposed categories serve well the needs that originated this study and are an appropriate framework for health care management purposes. In fact, the Colombian Ministry of Health has used it as an input for telemedicine and first infancy projects and health care reform. Its main conclusion is that health cannot be worked using political divisions. It is fundamental to use supply, demand and context criteria to determine regions useful for policymakers.

## HEALTH CARE USE & POLICY STUDIES – Drug/Device/Diagnostic Use & Policy

### PHP7

#### UNDERSTANDING STAKEHOLDER PERSPECTIVES ON MEDICARE'S COVERAGE WITH EVIDENCE DEVELOPMENT (CED) POLICY

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**OBJECTIVES:** To understand key stakeholder recommendations for the Centers for Medicare & Medicaid Services (CMS) regarding the application of its CED policy, the outcome of national coverage determinations (NCD) in which Medicare makes coverage contingent on additional evidence collection through a registry or prospective trials, and identify primary concerns with the policy across various stakeholders. **METHODS:** The authors analyzed stakeholder comments submitted to CMS during a public comment period on draft updates to the agency's 2006 CED policy. The comment period was from November 29, 2012 to January 28, 2013. Comments were retrieved from CMS' Medicare Coverage Database and assessed to understand stakeholder positions on issues related to the CED process. **RESULTS:** Of the 27 stakeholders who submitted comments to CMS, over half were from the life sciences industry. The majority of stakeholders called for CMS to provide more clarity on how the agency plans to address operational issues with CED implementation. Stakeholders who may be impacted by the issuance of a CED, such as manufacturers, are seeking greater transparency from CMS on policies and processes for applying CED as well as greater clarity on the parameters for executing CED studies. Specifically, 17 stakeholders called on CMS to prohibit CED at the local level and restrict its application to the NCD process while 12 stakeholders recommended CMS to provide clear timelines for the duration of CED studies. In addition, 11 stakeholders requested clarity from CMS on how it intends to collaborate with the Food and Drug Administration (FDA) on post-market evidence requirements, urging that CED should not duplicate or replace FDA's authority. **CONCLUSIONS:** Going forward, CMS will likely continue to invoke CED with increasing frequency and potentially on a broader range of products. Therefore, clearer guidance from CMS is critical to ensuring continued stakeholder engagement through Medicare's coverage determination process.

### PHP8

#### A LONG WAR BEGINS: BIOSIMILARS VERSUS PATENTED BIOLOGICS – A RETROSPECTIVE ANALYSIS OF THE EU-5 AND JAPANESE ERYTHROPOIETINS MARKETS

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**OBJECTIVES:** Analyze factors influencing Erythropoietins (EPO) biosimilars (copies of patented EPO) (BIOSIM-EPO) uptakes in key global markets. Identify, if possible,

country profiles where BIOSIM-EPO have taken market shares. **METHODS:** Countries inclusion criteria: legal definition and regulatory framework for biosimilars close to the EU ones; at least 3 years of experience with BIOSIM-EPO in 2012; national biological market value higher than US\$ 2.5 billion. Factors evaluated: national EPO market sizes, EPO retail/hospital distribution mixes, existence of policy incentives that promote BIOSIM-EPO prescriptions or substitution and BIOSIM-EPO prices relative to reference EPO. Data on medicine volumes, values and ex-manufacturer prices for all EPOs (alfa, BIOSIM-EPO (EPO alfa biosimilar), beta and second-generation ones) were provided by IMS Health. Volumes were calculated in DDD (Defined Daily Doses) and prices in euros per DDD. Data were available from 2007 until 2012. **RESULTS:** EU-5 and Japan have been included. Germany: small-sized market, dominant retail market distribution, incentives to prescribe BIOSIM-EPO (quotas) and to substitute patented for 'bioidenticals' EPO, high BIOSIM-EPO uptakes (30.4% in 2012). Spain and Italy: medium-sized markets, dominant hospital distribution, no incentives, 11.5% and 8.6% BIOSIM-EPO uptakes respectively. Japan: the largest market, mixed distribution channels, no incentives, 6.8% BIOSIM-EPO uptake. France: large-sized market, dominant retail market distribution, no incentives, 5.8% BIOSIM-EPO uptake. The UK: the smallest market, mixed distribution channels, no incentives, 2.0% BIOSIM-EPO uptake. The price differences between BIOSIM-EPO and their reference play no role at a global level (e.g. -10.8% in Germany and -26.9% in Japan). **CONCLUSIONS:** This study proved that EPO markets are highly country specific. There is no single specific profile for countries in which BIOSIM-EPO have significantly penetrated the market. Providing national prescription and substitution incentives is the only determining factor for BIOSIM-EPO uptakes. National EPO market sizes, EPO retail/hospital distribution mixes and BIOSIM-EPO prices relative to reference EPO are not significant factors.

### PHP9

#### MEDICAL DEVICES IN JAPAN – A MARKET ACCESS LABYRINTH?

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**OBJECTIVES:** With a total volume of €24 billion a year, Japan is the world's second largest medical device market behind the US. It imports about 35% of the medical devices from abroad. Although imports have been increasing steadily over the past years, Japan still struggles to have similar access to advanced medical devices as the US and Europe. This research aimed to have a closer look at the Japanese medical device market, and further explore access barriers. **METHODS:** This research was conducted through in-depth secondary research and interviews with a variety of stakeholders including payers, academics, and KOLs in Japan. **RESULTS:** Unlike most markets where an FDA or CE mark is sufficient, medical devices in Japan require a separate in-country regulatory approval before reimbursement. Not only is this process long (approximately 2.2 years) but the requirements are much more stringent compared to the US or EU, often requiring local clinical data. This has resulted in many large med-tech companies staying away from the Japanese market. **CONCLUSIONS:** It is important for foreign manufacturers to understand the implications of the Japanese regulatory barriers and address them in their foreign market strategies allowing them to assess product viability early on.

### PHP10

#### PRICE DYNAMICS OF EXTERNAL REFERENCE PRICING-BASED SYSTEMS IN EUROPE

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**OBJECTIVES:** Concerns due to external reference pricing (ERP) have been expressed by industry regarding spill-over effects. It is also often argued that ERP can lead to a downward price convergence. The objective of this project was to gain better understanding of price dynamics of ERP-based systems using a simulation model. **METHODS:** A simulation model (developed for the EU Commission) was built to simulate the impact of ERP as main criterion to set drug price across 28 European Union Member States, Iceland, Norway and Switzerland. Base case scenario simulated ERP price for a fictitious drug based on real ERP characteristics. Twenty fictitious scenarios simulated ERP price when introducing changes in ERP characteristics and/or exogenous effects such as genericisation, changes in exchange rates, price cuts. These scenarios were chosen based on the potential rapid and important price erosion attributed to ERP. Impacts of these scenarios were classified depending on changes in average drug price versus the base case. **RESULTS:** Applying solely ERP led to a low average drug price decrease (about 15% at 10 years), with an apparent equilibrium reached in approximately 7-8 years. Price differentials between countries remained substantial over 10 years (about 30%), suggesting a limited impact of ERP in price convergence. Even if impact differed depending on scenarios, all tested scenarios induced price decreases and demonstrated the spill-over effects of ERP. Frequent price revisions, iterative price cuts, large country baskets, price calculation methods, genericisation impact and prices' sources were among the most influent parameters on the evolution of the drug price over time through ERP-based systems. The repetition and combination of various policies generated average price decrease of 92% at 10 years. **CONCLUSIONS:** This study is the first that quantifies the impact of various ERP policies on price erosion. This is a useful tool to support policy decision making.

### PHP11

#### TIME LAGS FROM FDA DRUG APPROVAL TO PUBLICATION OF COST-UTILITY ANALYSIS

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**OBJECTIVES:** Cost-utility analysis (CUA) provides valuable information on the value of medical technology and is used by many payers to inform coverage and

reimbursement decisions. Our objective was to evaluate the lag between a drug's FDA approval and the publication of the first published CUA evaluating the product. **METHODS:** We used the FDA's website to identify newly-approved drugs from 2000-2010 (n=342). For each drug, we searched the Tufts Medical Center Cost-Effectiveness Analysis Registry and the NHS Economic Evaluation Database for CUAs evaluating the drug for the corresponding FDA-approved indication. We included drugs with a corresponding CUA in our dataset. When multiple CUAs for a drug were available, we included the CUA with the earliest publication date. We used multivariate regression to determine factors associated with time to CUA publication (years). Independent variables included drug approval year, study funder, i.e., whether the CUA was supported by industry, and whether the FDA assigned the drug priority review status. **RESULTS:** One hundred and fifty-six (45.6%) drugs in our sample had a corresponding CUA. Average time to CUA publication was 4 years (standard deviation 2.3 years). We divided drug approvals into three time intervals; 2000-2002 (mean time to CUA publication=5.3; SD=2.4), 2003-2006 (mean=3.9; SD=2.1) and 2007-2010 (mean=2.4; SD=0.97). We found that compared to CUAs for drugs approved from 2000-2002, time to CUA publication was 1.5 years shorter for drugs approved from 2003-2006 (p<0.001) and 3 years shorter for drugs approved from 2007-2010 (p<0.0001). Source of study support and FDA priority review status were not significantly associated with time to publication. **CONCLUSIONS:** For FDA-approved drugs with a corresponding CUA, we found a substantial time lag between FDA approval and CUA publication, suggesting that decision-makers are making important drug coverage and reimbursement decisions without published cost-effectiveness evidence available. However, the time to CUA publication appears to have declined over time.

#### PHP12

##### THE TREND OF PRICE LEVEL FOR ANTI-INFECTIVE DRUGS IN CHINA: AN EMPIRICAL STUDY BASED ON MULTIPLE INDEX METHODS

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**OBJECTIVES:** To measure the trend of price level for anti-infective drugs in Tianjin, China from 2006 to 2010 using multiple index methods and to explore measurement bias induced by index methods and measurement units. **METHODS:** Data were extracted from inpatient claims in Tianjin Urban Employee Basic Medical Insurance database from 2006 to 2010. Laspeyres, Paasches, Fisher and chained Fisher index methods were employed to measure the price level. Price indices were calculated both at molecule level (defined by active ingredient) and product level (defined by molecule, strength, preparation and manufacturer). Units of quantity and price were defined as per DDD (Defined Daily Dose), per milligram of active ingredient, and per minimum unit separately to calculate the indices. **RESULTS:** At product level, 367 constantly used products (26% of total 1422 products) were included in unchained indices and 1041 products (73% of total products) were included in chained Fisher indices. The results of multiple indices consistently indicated that the price level decreased and the decreasing range indicated by different index methods were from 16% (Laspeyres-unit index at molecule level) to 27% (Laspeyres-DDD index at product level). The price indices at molecule level decreased slower than the counterparts at product level (22% vs. 25% in chained Fisher-DDD index). At molecule level, price indices based on per DDD decreased faster than per mg and per unit (22%, 21% and 18% in chained Fisher). Laspeyres indices decreased slower than Paasches at molecule level while the contrary was the case at product level. The results from chained Fisher and unchained counterparts were similar (25% vs. 26% at product level). **CONCLUSIONS:** The price level of anti-infective drugs decreased heavily in Tianjin, China. The chained indices were similar to the unchained counterparts which suggested that the price of newer and older products decreased at similar rate.

#### PHP13

##### PERFORMANCE EVALUATION OF THE ESSENTIAL MEDICINES SYSTEM IN CHINA BASED ON DATA ENVELOPMENT ANALYSIS: A CASE STUDY IN SICHUAN PROVINCE

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**OBJECTIVES:** To establish performance evaluation model of the Essential Medicine System in China based on Data Envelopment Analysis (DEA), evaluate the relative efficiency of essential medicines system and analysis the main problem and impact factors on it. **METHODS:** 15 counties in Sichuan province were selected by stratified sampling as Decision Making Units (DMUs); for each county, 30% primary health care facilities, totally 284 facilities were involved as sample. Questionnaire survey was conducted to collect data of input and output indicators in 2010 and 2011 from sample facilities. 3 input indicators and 4 output indicators were set based on literature review, WHO's National Drug Policies Monitoring Indicators and experiential principle of DEA. Excel 2007 was used to encode data, DEAP 2.1 software was used to conduct CRS - CCR and VRS - BCC Data Envelopment Analysis, SPSS16.0 was used to conduct T-test and multiple linear regression analysis to exam the statistic difference between 2010 and 2011, and the influencing factors of efficiency. **RESULTS:** For input indicators, the average special funds of Essential Medicine System (x1) in 15 counties was raised from 0.52 million US\$ in 2010 to 0.69 million US\$ in 2011 the average number of essential medicines (x2) and drug delivery companies (x3) raised as well. For output indicators, average outpatient cost per visit (y1) and inpatient cost per admission (y2) decreased, while the outpatient visit times (y3) and discharge numbers (y4) kept not increasing as expected. The overall efficiency of Essential Medicines System in Sichuan province in two years were in relatively high level (0.908 in 2010 and 0.832 in 2011). Analysis on technical efficiency, scale efficiency, and return to scale showed the main existing problem was insufficient utilization of input health care resource. **CONCLUSIONS:** The effectiveness of implementation of Nation Essential Medicine System has been displayed, but health care resources should be adjusted and utilized rationally to improve the overall efficiency.

#### PHP14

##### DIVERGENT EVIDENCE REQUIREMENTS COMPARING THE AUTHORIZATION AND REIMBURSEMENT PROCESSES OF HIGH-RISK MEDICAL DEVICES - THE EUROPEAN SITUATION

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**OBJECTIVES:** In the last decade awareness has been raised due to unsafe and dangerous devices entering the European market, putting patient safety at stake. Consequently, evidence requirements may not be enough to ensure a high-quality and safe provision of medical devices in Europe. This research aims at exploring the authorization and reimbursement processes and the associated evidence requirements comparing four high-impact regions Europe, United States, Australia and Canada. **METHODS:** First, we performed a literature search about the authorization and reimbursement in the four high-impact regions. Second, seven high-risk medical devices were chosen as examples and current authorization and reimbursement status were assessed. Information was extracted from publicly available summaries, from PubMed, and from the clinical trial database (clinicaltrials.gov), supplemented by the worldwideweb. **RESULTS:** The evidence required for the authorization and reimbursement processes clearly differs in the four high-impact regions. All seven devices have been authorized in Europe, three in Australia, one in the United States, and one in Canada. Currently none of the seven devices is recommended for reimbursement in the four high-impact regions. **CONCLUSIONS:** Looking at the difference in evidence requirements, more harmonization, transparency and specific regulations are needed worldwide for the authorization and reimbursement of high-risk medical devices to ensure a high-quality and safe provision.

#### PHP15

##### OVERVIEW OF EXTERNAL REFERENCE PRICING SYSTEMS IN EUROPE

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**OBJECTIVES:** External reference pricing (ERP) is one of most common cost-containment tools used to reduce prices for in-patent pharmaceuticals in the European Union Member States (MS). The objective of this project was to provide an overview of ERP systems, both on processes and potential issues related to ERP systems in 31 European countries (28 EU MS, Iceland, Norway and Switzerland) (performed for the EU Commission). **METHODS:** A systematic structured literature review and consultation of representatives of competent authorities and international organizations were conducted to identify and characterize the use of ERP, to describe its impacts on the prices of pharmaceuticals and to discuss possible cross-country coordination issues in EU MS. **RESULTS:** All selected countries apply ERP except the UK and Sweden and 23 countries use ERP as main systematic criterion. ERP is based on legislated pricing rules with different levels of accuracy in the majority of European countries using ERP. ERP is applied either to all marketed drugs or to specific categories of medicines, mainly used for publicly reimbursed medicines. The number of reference countries included in the basket varies from 1 to 31. There is a great variation in calculation methods used to compute the price; 15 countries use average price, 7 countries use the lowest price, and 7 countries use other calculation methods. Among reported limitations of ERP application are reliable sources of price information, price heterogeneity, exchange rate volatility, and hidden discounts. Spill-over effects on other countries and downward price convergence have often been argued leading to pricing strategies from pharmaceutical companies. **CONCLUSIONS:** While ERP is widely used in Europe, processes and available price information vary from one country to another that may limit ERP application. Moreover, ERP spill-over effect is a major concern of pharmaceutical firms leading to implementation of the so-called "launch sequence strategies".

#### PHP16

##### THE ANALYSIS OF THE DRUG REIMBURSEMENT DECISIONS BEFORE AND AFTER THE POSITIVE LIST SYSTEM IN SOUTH KOREA

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**OBJECTIVES:** In Korea, the positive list system (PLS) was introduced in 2007 to ensure the good value for money in pharmaceutical expenditure. This study aims to investigate factors that are most influential in reimbursement decisions under the PLS. **METHODS:** To assess the 5 years operations and compare the results before and after the PLS, we analyzed the drug prices submitted from the companies, the reimbursement decisions made by Pharmaceutical Benefit Coverage Assessment Committee (PBCAC). We extracted data from published evaluation reports, PBCAC meeting minutes, and internal documents of Health Insurance Review and Assessment Service. **RESULTS:** Under the PLS, 71% of submitted drugs were recommended for reimbursement during January 2007- April 2012. For submissions demonstrated superiority or non-inferiority in clinical benefit, 79% of submissions were decided to be reimbursed. However, submissions with inferiority or uncertainties in clinical benefit were rejected regardless of the price. Comparing the negotiated price under the PLS to the relative price under the negative system, the negotiated price was 85% of the relative price. The probability of recommendation was high when ICER was under the GDP per capita, nevertheless submissions with high uncertainty in cost-effectiveness were rejected. Submissions which had low uncertainty and products for severe diseases or rare diseases were recommended for reimbursement despite ICER was high. **CONCLUSIONS:** This study confirmed clinical benefit was the main driver of the reimbursement decision making. Not only clinical benefit and cost-effectiveness but the disease severity, the uncertainty of evidence and reimbursement in other countries were also considered in the reimbursement decision making process. In addition, the drug prices were reduced a little after PLS introduced compared to those under the negative list system.